UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte HUBERT METZNER and HEINRICH SCHNEIDER

Appeal No. 2005-0192
Application No. 09/809,021

ON BRIEF

Before SCHEINER, MILLS and GRIMES, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 18, 19, and 35-38. Claims 20-34 are also pending but have been withdrawn from consideration by the examiner. Claim 18 is representative of the subject matter on appeal and reads as follows:

18. A thrombin preparation comprising thrombin and a noncovalently binding inhibitor of thrombin activity as stabilizer, wherein the thrombin preparation is suitable for therapeutic purposes.

The examiner relies on the following references:

Altshuler	4,363,319	Dec. 14, 1982
Hanada et al. (Hanada)	5,945,103	Aug. 31, 1999

Lorne et al. (Lorne), "Transfusion Technology : Purification of Human Thrombin by Affinity Chromatography For Its Use in Biological Glue Preparations," Rev. Fr. Transfus. Hemobiol., Vol. 32, pp. 391- 400 (1989)

Allary et al. (Allary), "Isolation by Affinity Chromatography, on Silica Support, of Human Thrombin for Its Use in Biological Glue Preparations," Annales Pharmaceutiques Francaises, Vol. 48, No. 3, pp. 129-135 (1990)

Brezniak et al. (Brezniak), "High Stability of Dilute Human α-thrombin in Salt Solutions," Blood Coagulation and Fibrinolysis, Vol. 5, pp. 847-848 (1994)

Claims 18, 35, and 37 stand rejected under 35 U.S.C. § 102(b) as anticipated by either Allary or Lorne.

Claims 18, 19, and 35-38 stand rejected under 35 U.S.C. § 103 as obvious in view of either Allary or Lorne, combined with Hanada, Brezniak, and Altshuler.

We affirm.

Background

"Since it became possible to produce thrombin commercially, several applications thereof have emerged. The main applications . . . are, besides diagnostic purposes, the use as a local hemostatic or as a component of a tissue glue together with a fibr[in]ogen-containing component." Specification, paragraph [0002].[1]

"For formulation of the thrombin preparation as a component, which is stable and storable in the liquid and, where appropriate, also in the frozen state, for use in a tissue glue or on its own as a local hemostatic, a buffer should be used to adjust to a pH of

about 5.0 to 8.0. To achieve the desired effect on use and for stabilization, then a soluble calcium salt, sodium chloride, a sugar or a pure alcohol and/or an amino acid . . . is added to the preparation. This results in good stabilities in the liquid and/or frozen state for a storage time of 12 months or more." Paragraph [0016].

"It has also emerged that addition of substances which inhibit noncovalently the thrombin activity in vitro can seemingly only increase the stability even further, especially at room temperature, by diminishing the autolysis of thrombin. Suitable substances for this purpose are compounds such as benzamidine or p-aminobenzamidine." Paragraph [0017].

"The thrombin preparations produced by the described process can be employed inter alia as components of a fibrin glue [in combination with fibrin and optionally factor XIII]." Paragraph [0020]. "Finally, the thrombin concentrates produced according to the invention can also be employed alone or in combination with carrier materials as agent for local stoppage of bleeding." Paragraph [0021].

Discussion

The claims stand or fall together. Appeal Brief, page 5. Since the broadest claim subject to each rejection is claim 18, we will consider that claim as representative. Claims 19 and 35-38 will stand or fall with claim 18.

Claim 18 is directed to a thrombin preparation which is "suitable for therapeutic purposes," comprising thrombin and "a noncovalently binding inhibitor of thrombin

[1] The instant application's official Image File Wrapper contains images of very poor quality; nearly every page is partially illegible. Therefore, our citations to the specification refer to the version of the application that was published on October 25, 2001 as Publication No. 2001/0033837.

activity as stabilizer." The examiner rejected some of the claims as anticipated and all of the claims as obvious in view of the prior art.

1. Anticipation

The examiner rejected claims 18, 35, and 37 as anticipated by either Allary or Lorne, stating the rejection as follows:

> The references each teach that thrombin is eluted off a benzamidine-Sepharose column. Thrombin and benzamidin[e] would be together in the eluate. Since they elute using benzamidine in a competitive elution then a complex of thrombin-benzamidine as in the present claims would have been formed.

Examiner's Answer, page 4.

We agree with the examiner that the experiments described by either Allary or Lorne appear to result in a composition meeting all of the limitations of instant claim 18. Since the references both seem to describe the same experimental procedures, we will limit our discussion to Lorne. Lorne discloses purification of thrombin by affinity chromatography. See pages 5-7.[2] Benzamidine was immobilized on dextran-coated silica beads (Spherodex) and placed inside a column. Page 5. Samples containing thrombin were then injected into the column (id.) and the thrombin was allowed to adsorb onto the immobilized benzamidine (page 6). After the column was washed with buffer to eliminate nonadsorbed proteins, the thrombin was eluted from the column using, in one experiment, a solution comprising 15 mM benzamidine. Page 7, lines 5-6.

[2] Our citations to Lorne refer to the English-language translation, of record. We note that the examiner's statement of the rejection referred only to "Allary et al. (abstract) or Lorne et al. (abstract)." Examiner's Answer, page 4. However, as Appellants noted, the examiner made of record full-text translations of the Allary and Lorne references at the time the Examiner's Answer was mailed. Reply Brief, page 2. We also note that Appellants apparently had access to their own full-text translations prior to writing the Appeal Brief, since partial translations were included in the brief and Appellants offered to provide the full-text

Lorne describes the results of the experiment:

> Benzamidine at the concentration of 15 mmol/l also led to elution of the thrombin. The results are comparable to those obtained with arginine methylester in terms of specific activity (1450 NIH units/mg), yield (approximately 78%), and electrophoretic purity. . . .
>
> Regardless of the elution method selected, the final recovery of this thrombin obtained by chromatography must be done via a preliminary dialysis or ultrafiltration in an NaCl 1 M medium in order to dissociate the complex formed with the elution agent. Next, the salt will be eliminated by dialysis against water and glucose at 10 g/l in order to place the protein in good conditions to lyophilize it.

Page 15.

Thus, the initial eluate described by Lorne (i.e., the eluate prior to the two dialysis treatments described in the last paragraph of the above quote) reasonably appears to be a thrombin preparation comprising enzymatically active thrombin as a complex with benzamidine.

Appellants do not dispute that Lorne's preparation comprises a complex of thrombin and benzamidine, but they argue that the preparation does not anticipate claim 18 because "[r]eview of the full documents shows that . . . neither Lorne nor Allary teaches a preparation comprising both 'thrombin' and a 'noncovalently binding inhibitor of thrombin activity' such that the overall composition with both ingredients is 'suitable for therapeutic purposes.'" Id., page 17. The phrase "suitable for therapeutic purposes," Appellants argue "mean[s] that it can be directly administered to a patient." Id., page 16.

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translations to the Board. See the Appeal Brief, page 17 (footnote 2). Since both Appellants and the examiner apparently considered and relied upon the full-text references, we will do so as well.

Appellants point to the chromatographic procedure used by Allary and Lorne and argue that

> there is no evidence that the eluates from either Lorne or Allary's columns are "suitable for therapeutic purposes" according to claim 18. . . . For example, they may contain unsuitable run-off from the SPHERODEX® columns or unsuitable buffer ingredients. Further, there is no evidence that the thrombin solutions in the chromatography procedure are suitably sterilized.

Id., page 18. Appellants also point to Lorne's disclosure that the thrombin-containing preparation eluted from the column is subjected to two steps of dialysis or ultrafiltration before it is in a form intended for administration to a patient. See id., paragraph bridging pages 17 and 18.

We agree that claim 18 requires the thrombin preparation to be "suitable for therapeutic purposes" and, therefore, the preparations disclosed by Lorne and Allary must meet this limitation in order to anticipate the claim. However, we do not agree that the prior art compositions fail to meet this limitation.

"It is axiomatic that, in proceedings before the PTO, claims in an application are to be given their broadest reasonable interpretation consistent with the specification and that claim language should be read in light of the specification as it would be interpreted by one of ordinary skill in the art." In re Sneed, 710 F.2d 1544,1548, 218 USPQ 385, 388 (Fed. Cir. 1983) (citation omitted).

In this case, the specification does not define (or even contain) the phrase "suitable for therapeutic purposes." However, the specification describes the claimed thrombin-containing preparation as "use[ful] as local hemostatic or as component of a tissue glue together with a fibr[in]ogen-containing component." Page 1, paragraph

[0002]. Therefore, we will accept, for argument's sake, Appellants' position that the claimed preparation must be in a form that can be directly administered to a patient.

In addition, since the uses disclosed in the specification rely on thrombin's enzymatic activity as part of the blood-clotting process, the claimed preparation must apparently contain enzymatically active thrombin in order to be suitable for therapeutic purposes. We do not, however, interpret the claim to require that the preparation be stable when stored in liquid form, or that it be virus-free, or that it be sterile. While those properties may be desirable for a commercial product, the absence of such properties would not render the preparation therapeutically ineffective. Therefore, they are not required by the phrase "suitable for therapeutic purposes" when that phrase is given its broadest reasonable interpretation in light of the specification.

Based on this interpretation of the claim language, the prior art preparations reasonably appear to be "suitable for therapeutic purposes." Lorne discloses that the thrombin in the eluate had a specific activity of "1450 NIH units/mg"; therefore, the thrombin was enzymatically active. Although Lorne suggests that the thrombin- and benzamidine-containing eluate should be subjected to a two-step dialysis procedure, those dialyses are intended "to place the protein in good conditions to lyophilize it." Page 15. Lorne does not disclose or suggest that the dialyses are required in order to make the thrombin-containing solution therapeutically effective.

In fact, Lorne provides evidence that the standard for therapeutic efficacy is rather low. Lorne teaches that the standard thrombin used in fibrin glues "is of animal origin, specifically equine or bovine." Page 3. Thus, a thrombin-containing preparation

apparently need not even contain human thrombin in order to be "suitable for therapeutic purposes."

We conclude that the compositions disclosed by Lorne and Allary reasonably appear to meet all of the limitations of instant claim 18. The burden therefore shifts to Appellants to provide evidence to the contrary. See In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977) ("[W]here the Patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on.").

Appellants have provided no evidence to show that the thrombin- and benzamidine-containing eluate disclosed by the prior art is not "suitable for therapeutic purposes." Since the prior art composition reasonably appears to meet all the limitations of instant claim 18, and Appellants have provided no evidence that it does not, we affirm the rejection of claim 18 as anticipated by either Allary or Lorne. Claims 35 and 37 fall with claim 18.

2. Obviousness

The examiner rejected claims 18, 19, and 35-38 as obvious over either Allary or Lorne, combined with Hanada, Brezniak, and Altshuler. As noted above, all of the claims stand or fall together. Therefore, we need only consider claim 18; claims 19 and 35-38 stand or fall with claim 18.

We have already concluded the claim 18 is anticipated by either of Allary or Lorne. Therefore, claim 18 is also obvious in view of either Allary or Lorne, standing

alone. See In re May, 574 F.2d 1082, 1089, 197 USPQ 601, 607 (CCPA 1978) (Anticipation is "the epitome of obviousness.").

Appellants' arguments in response to this rejection are the same as in response to the rejection under 35 U.S.C. § 102, and have been adequately addressed above. The rejection of claim 18 as obvious in view of either Allary or Lorne, combined with Hanada, Brezniak, and Altshuler, is affirmed. Claims 19 and 35-38 fall with claim 18.

Other Issues

Appellants filed an Information Disclosure Statement on September 8, 2003, which does not appear to have been considered by the examiner. On return of this application, the examiner should review the IDS and treat is as appropriate under 37 CFR §§ 1.97 and 1.98.

Summary

The prior art reasonably appears to disclose a composition meeting the limitations of claim 18 and Appellants have provided no evidence to the contrary. We therefore affirm the rejection of claim 18 as both anticipated and obvious. The remaining claims fall with claim 18.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Toni R. Scheiner)
Administrative Patent Judge)
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Demetra J. Mills) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND
) INTERFERENCES
Eric Grimes)
Administrative Patent Judge)

EG/dym

Finnegan, Henderson, Farabow
Garrett & Dunner LLP
1300 I Street, NW
Washington, DC 20005